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NO DRAWINGS

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COMPLETE SPECIFICATION

Stabilized Multivitamin Compositions containing Vitamin B_{12}

We, THE VITARINE COMPANY, INC., a corporation organized under the laws of the State of New York, United States of America, and having principal offices at 636, Eleventh Avenue, City of New York, New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a new and improved Vitamin B_{12} composition and a new and improved method of stabilizing Vitamin B_{12}.

In solid condition, Vitamin B_{12} (also known as cyanocobalamin) is in the form of hygroscopic, dark-red crystals which are stable in solid form. One gram thereof dissolves in about 80 cc. of water at 25° C.

Said Vitamin B_{12} is substantially stable in solid form and in aqueous solution if dissolved without other vitamins, with maximum stability in a pH range of 4.5 to 5.

When the aqueous solution, in addition to said Vitamin B_{12} contains other dissolved vitamins, particularly dissolved Vitamin C (ascorbic acid) B_1 and niacinamide, the dissolved Vitamin B_{12} is unstable.

In making an aqueous solution of Vitamin B_{12} with other vitamins, it is known to add various additional ingredients, such as buffers, preservatives, flavoring agents, etc. These additional ingredients may include liver extract which may contain iron in combined form, or mineral salts which may contain iron in combined form. The liver extract or said mineral salts are added for therapeutic purposes.

The technical literature states that Vitamin B_{12} is incompatible with ferrous sulfate and is incompatible with Vitamin C, thiamine plus niacinamide and any potent reducing substance. Ferrous compounds in solution with Vitamin B_{12} cause rapid destruction of Vitamin B_{12} when present in therapeutic concentrations. This has been verified by several investigators. Ferrous compounds in therapeutic amounts are contra-indicated for inclusion even in solid formulations in combination with Vitamin B_{12} due to the deleterious effect on Vitamin B_{12} stability.

According to this invention, on the other hand, it has been discovered that a mixed aqueous solution of Vitamin B_{12} and another vitamin or other vitamins, particularly a mixed aqueous solution containing Vitamin B_{12} and Vitamin C, can be stabilized by all iron compounds or salts. Thus, in accordance with the present invention, aqueous products containing various vitamins including Vitamin C and Vitamin B_{12} in stable form suitable for oral or parenteral administration are produced by incorporating therewith a minor, non-therapeutic proportion of an iron compound or compounds or salts thereof. The degree of stabilization of Vitamin B_{12} achieved depends on the particular iron compound or salt used, the concentration of iron compound or salt used, especially in comparison with the concentration of Vitamin B_{12} which must be stabilized, and the nature and concentrations of the other substances present in the solution, but in general the amount of iron to be employed is in the range of 15 to 2500 micrograms per milliliter, calculated as atomic iron for solutions containing from 0.5 to 25 micrograms of Vitamin B_{12} per milliliter. The stabilizing iron compounds or salts are used in this invention as stabilizing agents, and not as therapeutic agents, and, accordingly, their concentration is below the therapeutic level. As indicated, while the use of therapeutic concentrations of ferrous compounds is contra-indicated, yet, in very low concentrations these same ferrous compounds will, unexpectedly, stabilize Vitamin B_{12} in the presence of other substances normally considered deleterious to Vitamin B_{12} stability (i.e., Vitamin C, Thiamine and Niacinamide). These concentrations are far below the

amounts of iron commonly used in preparations to supply the minimum daily therapeutic dose of iron (i.e., for hypochromic anemias, etc.).

These stabilizing iron compounds or salts of the invention are exemplified, without limitation thereto, by the following: iron peptonate, ferric amonium citrate, ferric chloride, ferrous gluconate, ferric glycerophosphate, ferric sulfate, ferrous sulfate, ferric oxide, ferrous oxide, ferric or ferrous complexes of such substances as ethylene diamine tetracetic acid and its salts.

It has also been discovered that the stabilizing effect begins at a certain minimum concentration of iron (calculated as atomic iron) in the solution; that said stabilizing effect increases up to a certain maximum concentration of iron, calculated at atomic iron, and that the stabilizing effect decreases when said maximum concentration is exceeded, also calculating the iron as atomic iron. Also, the stabilizing effect depends upon the respective iron compound, in addition to its concentration. The stabilizing effect also depends upon the dissolved ingredients other than dissolved Vitamin B_{12}, which are dissolved in the solution.

The Vitamin B_{12} may be admixed with the stabilizing agent in solid form, and the mixture may be dissolved in water for use.

Without limitation thereto, the invention is illustrated by the following Examples which show some embodiments of, and some best ways for carrying out the invention. All pH measurements mentioned herein are made at 20° C.—30° C., by means of the glass electrode.

In the following Examples 1—9 two aqueous solutions of the following composition were used:

SOLUTION I.

Each 5 cc. of this solution contained:

Vitamin A	3000 U.S.P. Units
Vitamin D	1000 U.S.P. Units
Vitamin B_1	1.5 mg.
Vitamin B_2	1.2 mg.
Vitamin B_{12} (cyanocobalamin)	6 mcg.
Vitamin C (Ascorbic Acid)	60 mg.
Niacinamide	10 mg.

To this solution suitable flavoring agents (such as citric acid, sugar, saccharin, propylene glycol and oil of lemon), solubilizers for Vitamin A and Vitamin D (such as polysorbate 80), preservatives (such as butyl parahydroxybenzoate or sodium benzoate) and thickeners (such as carboxymethyl cellulose) can be added.

SOLUTION II.

With the exception of the Vitamin B_{12} concentration, this solution had the same composition as the above described Solution I. Each 5 cc of solution II contained 3 mcg. of Vitamin B_{12} (cyanocobalamin), i.e. half of the amount present in Solution I.

These solutions were subdivided and iron peptonate or ferric ammonium citrate were added in the amounts stated hereinafter to separate portions, which were then stored at 37° C. for a period of three weeks. After this period the Vitamin B_{12} concentration of the solutions was asayed by the microbiological method described in U.S.P. XIV 3rd Supplement. This method, as normally used, is accurate with an error of ±10—20%, which is a reasonable error for a microbiological assay of this type.

TABLE 1

No. of Example	Solution Used	Stabiliser Used	Amount of Stabiliser	B_{12} Assay After Storage at 37° C.
1	I	iron peptonate	0.1 mg./cc.	7.05 mcg./5 cc.
2	I	„ „	1.0 „	5.46 „
3	I	„ „	10.0 „	6.50 „
4	I	ferric ammonium citrate	0.1 „	4.35 „
5	I	„	1.0 „	2.58 „
6	I	„	10.0 „	2.04 „
7	II	iron peptonate	10.0 „	3.19 „
8	I	none	—	1.78 „
9	II	none	—	0 „

In Examples 10—12, a solution containing in each cc. the following vitamins was used:

Vitamin A (palmitate)	8330 U.S.P. Units
Vitamin D	2000 U.S.P. Units
Vitamin B_1	3.33 mg.
Vitamin B_2	0.83 mg.
Vitamin B_6	1.67 mg.
Vitamin C	100 mg.
Niacinamide	16.67 mg.
Pantothenic acid (as Panthenol)	5 mg.
Choline Chloride	12 mg.
Inositol	7 mg.
Vitamin E (Mixed Tocopherols)	1.67 mg.

This solution also contained as flavoring agents: glycerine, propylene glycol, saccharin, raspberry flavor; as solubilizer for Vitamins A, D and E: polyoxyethylene sorbitan monolaurate, or polysorbate 80; and, as preservative: methyl parahydroxybenzoic acid and/or sodium benzoate.

The solvent used was a mixture of glycerol, propylene glycol and distilled water. To the solution thus prepared Vitamin B_{12} (cyanocobalamin) was added to produce a concentration of approximately 14 mcg. per cc. The resulting liquid, which is denoted hereinafter "Solution III" was subdivided into several portions, to which the stabilizers listed in Table 2 were added and which were then stored at 37° C. for three weeks. After storage the Vitamin B_{12} content was assayed with the following results:

TABLE 2

No. of Example	Solution Used	Stabiliser Used	Amount of of Stabiliser	B_{12} Assay After Storage at 37° C.
10	III	iron peptonate	10 mg./cc.	14.65 mcg./cc.
11	III	ferric ammonium citrate	10 „	11.40 „
12	III	none	—	0 „

In Examples 13—19 an aqueous solution denoted hereinafter "Solution IV" was used, 1 cc. of which contained the following vitamins:

B_1	100 mg.
B_2	1 mg.
B_6	2 mg.
B_{12} (Cyanocobalamin)	23 mcg.
Niacinamide	100 mg.
Pantothenic Acid (Panthenol)	10 mg.
Benzyl Alcohol	1.5% (based on weight/volume)

This solution was subdivided into several portions, to which the stabilizers listed in Table 3 were added. The solutions were stored at 37° C. for three weeks and after that time their Vitamin B_{12} content was assayed. The results are shown in the following Table:

TABLE 3

No. of Example	Solution Used	Stabiliser Used	Amount of Stabiliser	B_{12} Assay After Storage at 37° C.
13	IV	iron peptonate	0.1 mg./cc.	25.2 mcg./cc.
14	IV	" "	1.0 "	19.1 "
15	IV	" "	10.0 "	18.1 "
16	IV	ferric ammonium citrate	0.1 "	19.9 "
17	IV	" "	1.0 "	16.5 "
18	IV	"	10.0 "	14.8 "
19	IV	none	—	0 "

In Examples 20—22, a solution denoted hereinafter "Solution V" was used, which contained the following ingredients in each one cc.:

Vitamin B_1	100 mg.
Vitamin B_2	1 mg.
Vitamin B_6	2 mg.
Niacinamide	50 mg.
Panthenol	10 mg.
Vitamin B_{12} (cyanocobalamin)	15 mcg.
Vitamin C	100 mg.
Buffers, preservatives, etc.	6% (based on weight/volume)
Distilled Water q.s.	

As buffers and preservatives, sodium citrate (2% w/v), benzyl alcohol (1% w/v) and gentisic acid ethanolamide (3% w/v) were present in the solution. The initial assay of the solution was 16.1 mcg. of Vitamin B_{12} per cc.

EXAMPLE 20.

To a portion of solution V, 0.5 mg./cc. of iron peptonate was added and resulting solution was stored at 37° C. for three weeks. After such storage, the solution showed a Vitamin B_{12} assay of 15 mcg./cc. Since this solution originally had 15 micrograms of cyanocobalamin per cc., the microbiological assay showed a concentration of 100% of potency.

EXAMPLE 21.

To a portion of solution V, 12 mg./cc. of iron peptonate were added and the solution was then stored at 37° C. for three weeks. After storage, a Vitamin B_{12} assay of 7 mcg./cc. was found. Hence, in this case, the value of the cyanocobalamin found in the microiological assay was substantially 50% of the original concentration.

EXAMPLE 22.

After storage at 37° C. for three weeks without any addition, a portion of solution V showed a vitamin B_{12} assay of less than 1 mcg./cc.

In the preceding Examples 20—22 there is a demonstration of the decrease in stabilization of Vitamin B_{12} achieved when the concentration of iron compound more nearly approaches therapeutic levels. Solution V, which contains Ascorbic Acid, Thiamine and Niacinamide, etc., is normally considered a poor medium for Vitamin B_{12} stability, a view verified by Example 22. Addition of a small amount of iron compound (0.5 mg/cc. of iron peptonate) as in Example 20, produced a solution of good Vitamin B_{12} stability. A concentration of the same iron compound, as used in Example 21, showed a sharply decreased Vitamin B_{12} stability in comparison with Example 20. It is to be noted that the atomic iron concentration of Example 21 was 2 mg/cc. The normal human dose of this preparation is 1 cc. Therefore, this preparation supplies one-fifth the minimum daily adult iron requirement per dose. Yet, this concentration of iron, in relation to the other ingredients, produced a less satisfactory stabilization of Vitamin B_{12} than the much smaller amount used in Example 20. This serves to demonstrate that the peak of Vitamin B_{12}

stabilization is achieved with the addition of an iron compound in an amount far less than the therapeutic amounts.

EXAMPLE 23.

A starting solution corresponding to that used in the above Examples 10—12 was prepared, containing in each cc. the following vitamins:

Vitamin A (palmitate)	8330 U.S.P. Units
Vitamin D	2000 U.S.P. Units
Vitamin B_1	3.33 mg.
Vitamin B_2	0.83 mg.
Vitamin B_6	1.67 mg.
Vitamin C	100 mg.
Niacinamide	16.67 mg.
Pantothenic Acid (as Panthenol)	5 mg.
Choline Chloride	12 mg.
Inositol	7 mg.
Vitamin E (Mixed Tocopherols)	1.67 mg.

This solution also contained as flavoring agents: glycerine, propylene glycol, saccharin, raspberry flavor; as a solubilizer for Vitamins A, D, E: polyoxyethylene sorbitan monolaurate, or polysorbate 80; and, as a preservative: methyl parahydroxybenzoic acid and/or sodium benzoate. The solvent was a mixture of glycerol, propylene glycol and distilled water.

The resulting solution was divided into 3 portions, and to these portions Vitamin B_{12} was added as follows:

(a) To the first portion 10 mcg. per cc. of Vitamin B_{12} activity, Type S (Merck) was added, i.e. Vitamin B_{12} consisting of a semi-refined B_{12} fermentation product, whose activity is due entirely to cyanocobalamin and which is blended with inert ingredients suitable for bulk handling to a concentration of 1 mg. Vitamin B_{12} activity per gram of gross weight.

(B) To the second portion, 10 mcg. per cc. of Vitamin B_{12} activity was added, in the form of oral grade solids (Calco), consisting of a concentrate in semi-purified state of B_{12} activity components obtained from microbiological fermentation, suitable for oral use and blended with inert ingredients to an activity of 1 mg. of B_{12} per gram of gross weight. This Vitamin B_{12} activity is composed of approximately 75—80% of hydroxy cobalamin, the balance being predominantly cyanocobalamin.

(c) To the third portion, 10 mcg. per cc. of Vitamin B_{12} activity was added in the form of U.S.P. crystalline cyanocobalamin.

Each of these portions (a), (b) and (c) was again subdivided into 3 parts and iron peptonate was added to some, in the amounts listed below. Assays were taken at the time of preparation and after storage for 3 weeks at 37° C. The results were as follows:

TABLE 4

Portion	Original Assay Vitamin B_{12}	Assays After 3 Weeks Storage at 37° C. With		
		0.0	0.1 mg./cc. of Iron Peptonate Added	1 mg./cc.
(a)	10.4 mcg./cc.	0	0	8.2 mcg./cc.
(b)	8.7 „	0	0	9.1 „
(c)	11.4 „	0	0	9.7 „

The above data show that 1 mg. per cc. of iron peptonate stabilizes each of the three types of Vitamin B_{12}, equally as well in the preparation herein described.

EXAMPLE 24.

A multivitamin solution containing in each cc. the following ingredients, was prepared:

Vitamin A (palmitate)	8300 U.S.P. Units
Vitamin D	2000 U.S.P. Units
Vitamin B_1	3.33 mg.
Vitamin B_2	0.83 mg.
Vitamin B_6	1.67 mg.
Vitamin C	100 mg.
Niacinamide	16.67 mg.
Pantothenic Acid (as Panthenol)	5 mg.
Vitamin E (Mixed Tocopherols)	1.67 mg.

In this preparation, which is similar to that used in the above Examples 10—12, with the omission of choline chloride and inositol, the same flavoring and solvent as in Examples 10—12 were used.

To this preparation Vitamin B_{12} (cyanocobalamin) was added to produce a concentration of about 4 mcg./cc. This solution denoted hereinafter Solution VI, was divided into 13 portions and to these portions iron compounds were added, as described below. After storage for 3 weeks at 37° C. the Vitamin B_{12} was assayed, and following results were obtained:

TABLE 5

Stabiliser Used (if any)	Amount of Stabiliser	Amount of Iron per cc.	B_{12} Assay After 3 Weeks Storage at 37° C.
(a) none	—	0	0
(b) ferric chloride	1 mg./cc.	200 mcg./cc.	2.24 mcg./cc.
(c) ferric chloride with beef peptone	1 „ 2 „	200 „	2.23 „
(d) ferrous gluconate	1 „	116 „	1.89 „
(e) ferrous gluconate with beef peptone	1 „	116 „	1.80 „
(f) ferric glycerophosphate	1 „	180 „	2.84 „
(g) ferric ammonium citrate	1 „	160 „	2.24 „
(h) ferric sulfate	1 „	280 „	3.35 „
(i) ferrous sulfate	1 „	200 „	2.76 „
(j) iron peptonate	0.01 „	1.6 „	0
(k) „ „	0.1 „	16 „	0
(l) „ „	1.0 „	160 „	1.38 mcg./cc.
(m) „ „	10.0 „	1600 „	4.18 „

The above results demonstrate that all of the iron compounds used have a stabilization effect on Vitamin B_{12} in this preparation, which contains Ascorbic Acid as well as Thiamine, Niacinamide, and other vitamins. Where no stabilizer is used the Vitamin B_{12} decomposes rapidly. The results with iron peptonate ("j" though "m") indicate that a minimum amount of iron is required to achieve Vitamin B_{12} stabilization in this preparation, and that this stabilization effect increases as the amount of iron increases within the range of concentrations tested in this experiment.

In certain types of multivitamin preparations it may be deemed inadvisable to add appreciable amounts of iron compounds which yield appreciable amounts of ferric or ferrous ions in solution (e.g., ferric chloride). This is due to the known adverse effect of ferric irons on the stability of certain vitamins (e.g. Vitamin A, Pyridoxine Hydrochloride, etc.). However, it is also well known that iron may still be present in such solutions if present in the form of complexes or chelates. These bind ferric and/or ferrous ions into soluble forms which are only very slightly dissociated into the ionic forms of iron. Several of the stabilizers used in the above examples are illustrations of such complexes (e.g., Ferric Ammonium Citrate. Iron Peptonate, etc.). One of the most effective of such chelating agents is ethylene diamine tetra-acetic acid and its salts [called EDTA or Versene (R)]. The word "Versene" is a registered Trade Mark. So effective is this agent that it has been recommended for use

as a stabilizer for B Complex, Ascorbic Acid, and other vitamin preparations to prevent the breakdown of these vitamins in the presence of ionic iron. It is often used as a stabilizer in such preparations because of this property. However, even in the presence of EDTA, iron compounds will still stabilize Vitamin B_{12} in multivitamin preparations. This unexpected and surprising effect is of great practical importance, since it enables the use of iron compounds in multivitamin preparations to stabilize Vitamin B_{12} and, yet, the iron is so effectively combined in the chelate form that there is excellent stability of the other vitamins in the preparation. This is illustrated in the following Example 25.

EXAMPLE 25.

A solution identical with the composition used in solution I and II was prepared, except that the Vitamin B_{12} (Cyanocobalamine) was initially 4.0 mcg./5 cc. This solution which is denoted hereinafter as Solution VII, was subdivided into several portions and the stabilizers and EDTA added as listed in Table 6. After storage for 3 weeks at 37° C. the Vitamin B_{12} was assayed and the following results were obtained:

TABLE 6

Portion	Stabiliser Used (if any)	Amount of Stabiliser	Amount of Iron per cc.	Amount of EDTA	B_{12} Assay After 3 Weeks Storage at 37° C.
(a)	none	0	0	0	1.1 mcg./5 cc.
(b)	none	0	0	1 mg./cc.	0.8 „
(c)	ferric chloride hexahydrate	0.5 mg./cc.	0.1 mg./cc.	1 „	3.6 „
(d)	ferric chloride hexahydrate	0.5 „	0.1 „	0	3.7 „
(e)	iron peptonate	0.6 „	0.1 „	1 mg./cc.	3.7 „
(f)	„ „	0.6 „	0.1 „	0	4.3 „
(g)	ferric ammonium citrate	0.7 „	0.1 „	1 mg./cc.	4.1 „
(h)	ferric ammonium citrate	0.7 „	0.1 „	0	4.0 „

From the above data in Table 6 it can be seen that the Vitamin B_{12} in this preparation (which contains Vitamins A, C, D, Thiamine, Niacinamide, and other vitamins) is unstable without the addition of any iron compound. Addition of any of the three types or iron compound used (completely ionized as ferric chloride, partly ionized as ferric ammonium citrate, or non-ionic as iron peptonate) will materially aid the stability of Vitamin B_{12}. Addition of EDTA without iron (Portion b) does not stabilize the preparation. The simultaneous addition of an iron compound with EDTA does not appreciably reduce the Vitamin B_{12} stabilizing effect of the iron compounds. It is to be noted that the amounts of EDTA added in each case are in excess of that required to chelate the entire amount of iron aded. In Portions (c), (e), and (g) the EDTA added was sufficient to protect the other vitamins from iron-produced break-down, so that no appreciable decrease of potencies of Vitamin A, Thiamine, Pyridoxine, Ascorbic Acid, Riboflavin, and other vitamins took place.

From the above data there can also be seen the principle of using an iron complexing agent to protect the vitamin components other than Vitamin B_{12} from incidental instability induced by the use of iron as a stabilizer. Aside from EDTA other complexing or sequestering agents may be used, either alone or in combination. Among the many suitable complexing agents for this purpose there may be mentioned the following: ethylene diamine beta ethanol triacetic acid and its salts [Versenol (R)] d-saccharic acid and its salts, cyanides (or ferro- or ferri-cyanides), salts of pyrophosphoric acid, hexametaphosphoric acid, tripolyphosphoric acid, lactobionic acid, tartaric acid, citric acid and dextran, algin, and similar

carbohydrate gel forms. Tests have demonstrated the utility of these complexing agents both in stabilizing vitamins other than Vitamin B_{12} against deterioration by the iron containing stabilizer, and at the same time not interfering with the desired stabilizing effect of iron for Vitamin B_{12}.

The tests previously stated herein apply to solutions whose solvent includes water, and in which the original concentration of the dissolved ascorbic acid is greater than the original concentration of the dissolved cyanocabalamin. In the tested solutions, the dissolved ascorbic acid was in sufficient concentration to produce decomposition of the dissolved cyanocobalamin, thus resulting in substantial or complete destruction of the cyanocobalamin, when determined by microbiological assay at the end of a storage period of three weeks at 37° C., in the absence of a suitable proportion of added stabilizing agent.

The solutions to which a stabilizer according to the present invention is added have a pH in the range of 3 to 7. For example, the pH of the above described solutions is as follows:

Solution	I	5.0
„	II	5.2
„	III	5.1
„	IV	4.3
„	V	4.5
„	VI	5.0
„	VII	5.0

It will be understood from the above that the present invention is applicable to all forms of Vitamin B_{12}, such as for example crystalline cyanocobalamin, non-crystalline semi-refined cyanocobalamin and semi-refined mixtures of cyanocobalamin and hydroxycobalamine.

It will also be understood that the invention is not limited to the specific materials, proportions, steps and other details specifically described above and can be carried out with various modifications without departing from the scope of the invention, as defined in the appended claims.

WHAT WE CLAIM IS:—

1. Process for producing an aqueous multivitamin product containing Vitamin B_{12} in stable form which comprises admixing an aqueous solution Vitamin B_{12}, at least one other vitamin normally incompatible with Vitamin B_{12}, and as a stabilizer an iron compound in an amount sufficient to provide from 15 to 2500 micrograms calculated as atomic iron per milliliter of solution for solutions containing from 0.5 to 25 micrograms of Vitamin B_{12} per milliliter.

2. Process according to claim 1 wherein Vitamin C is incorporated in the solution.

3. Process according to claim 2 wherein Vitamin C is employed in an amount which is normally destructive to the Vitamin B_{12} per se.

4. Process according to claim 1 wherein thiamine and niaminamide are incorporated in the solution.

5. Process according to the preceding claims wherein a complexing or sequestering agent is incorporated in the solution in an amount sufficient to provide a complex with the iron present in the solution.

6. Process according to the preceding claims wherein ethylenediamine tetraacetic acid or a salt thereof is incorporated in the solution in an amount sufficient to provide a complex with the iron present in the solution.

7. Process according to the preceding claims wherein the stabilizer is iron peptonate.

8. Process according to the preceding claims wherein the stabilizer is ferric ammonium citrate.

9. Process according to the preceding claims wherein the stabilizer is an iron complex of ethylenediamine tetraacetic acid.

10. Process for producing an aqueous multivitamin product containing Vitamin B_{12} in stable form, substantially as hereinbefore described with reference to Examples 1 to 7, 10 and 11, 13 to 18, 20 and 21, and 23 to 25 of the foregoing Examples.

11. A stabilized vitamin solution containing at least 0.5 micrograms of Vitamin B_{12} per milliliter, at least one other vitamin normally capable of causing deterioration of Vitamin B_{12} per se, and as a stabilizer an iron compound in an amount sufficient to provide from 15 to 200 micrograms calculated as atomic iron per milliliter of solution, for solutions containing from 0.5 to 25 micrograms of Vitamin B_{12} per milliliter.

12. A stabilized solution according to claim 11, wherein one or more of the vitamins, ascorbic acid, thiamine and niacinamide are present.

13. A stabilized solution according to claim 11 or 12, wherein the iron stabilizer is present in the form of a complex or chelate.

14. A stabilized solution according to claim 11 or 12, wherein the iron stabilizer is present as a complex with ethylenediamine tetraacetic acid.

15. A stabilized solution according to claim 11 or 12, wherein the iron stabilizer is iron peptonate.

16. A stabilized solution according to claim 11 or 12, wherein the iron stabilizer is ferric ammonium citrate.

17. A stabilized vitamin solution containing Vitamin B_{12} substantially as hereinbefore described with reference to Examples 1 to 7, 10 and 11, 13 to 18, 20 and 21, and 23 to 25 of the foregoing Examples.

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